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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/714,567

11/14/2003

Paul Wentworth

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EXAMINER

VENCI, DAVID J

ART UNIT

PAPER NUMBER

1641

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/714,567	<b>Applicant(s)</b> WENTWORTH ET AL.	
	<b>Examiner</b> DAVID J. VENCI	<b>Art Unit</b> 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on November 2, 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-3,5-13 and 15-44 is/are pending in the application.
- 4a) Of the above claim(s) 21-44 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3,5-13 and 15-20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-3,5-13 and 15-44 are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

**DETAILED ACTION**

***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 19, 2007, has been entered.

Claims 1-3, 5-13 and 15-44 are pending in this application. Claims 21-44 are directed to a non-elected invention and was withdrawn (implicitly) from further consideration pursuant to 37 CFR 1.142(b) in the Office Action dated May 25, 2005.

Claims 1-3, 5-13 and 15-20 are under examination.

**Specification**

The disclosure is objected to because of the following informalities:

Throughout the specification, reference to the conversion of “singlet oxygen” into “reactive oxygen species” appears repugnant to the art-recognized definition of “reactive oxygen species” because persons skilled in the art generally do not recognize “singlet oxygen” as a separate genus, but rather recognize that “singlet oxygen” belongs to the broader genus of “reactive oxygen species.” Furthermore:

On p. 24, lines 27-28, the phrase “[t]he role of the newly discovered chemical potential of antibodies [to generate reactive oxygen species] *in vivo* is dependent on the availability of the key substrate  $^1\text{O}_2^*$ ” (paraphrasing mine) is not clear in view of p. 18, lines 4-5 phrase “the term ‘reactive oxygen species’ means antibody-generated oxygen species”. The source of *in vivo*  $^1\text{O}_2^*$  is not clear.

On p. 30, line 13, the phrase “[i]n the present invention, the minimum requirements are singlet oxygen, an antibody reagent...” (paraphrasing mine) is not clear in view of p. 18, lines 4-5 phrase “the term ‘reactive oxygen species’ means antibody-generated oxygen species”. The source of *in vivo*  $^1\text{O}_2^*$  is not clear.

Appropriate correction is required.

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***Claim Rejections - 35 USC § 112 – first paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

***New Matter Rejection***

Claims 1-3, 5-13 and 15-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

As amended, claims 1 and 11 require detection of administered probes for "reactive oxygen species" which are oxidized by *in vivo* antibody-generated oxygen.

The specification does not describe such detection methods specific for administered probes for "reactive oxygen species" which are oxidized by *in vivo* antibody-generated oxygen.

Applicants are required to cancel new matter in response to this Office Action.

*Lack of Enablement*

Claims 1-3, 5-13 and 15-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.<sup>1</sup> The claims contain subject matter not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 1 requires, *inter alia*, detecting oxidized probes for "reactive oxygen species" (see Specification, p. 18, lines 4-5, "As used herein the term 'reactive oxygen species' means antibody-generated oxygen species"). Claim 1 invokes probes for "reactive oxygen species" which are oxidized by *in vivo* antibody-generated oxygen.

The specification describes *in vitro* detection of probes for "reactive oxygen species" which are *in vitro* oxidized by *in vitro* antibody-generated oxygen. Specifically, the specification teaches:

1. UV-irradiated antibody catalyzes formation of one or more Amplex® Red oxidants (see Fig. 3, □; see *also*, Fig. 7A; see *also*, Fig. 8, ●, △, □, ○; see *also*, Figs. 8B, 8C, 8E, 8F and 10B), tris carboxyethyl phosphine oxidants (see Figs. 12A, 12B and 12C, m/z = 265, 267), and indigo carmine oxidants (see Fig. 18B).
2. White light-irradiated hematoporphyrin catalyzes formation of one or more indigo carmine oxidants (see Fig. 19C), especially in the presence of an antibody electron donor (see Fig. 19 B).

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<sup>1</sup> According to the decision in *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), the factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

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3. UV-irradiated hematoporphyrin catalyzes formation of one or more Amplex® Red hydrogen peroxide products (see Fig. 5, ♦), especially in the presence of an antibody electron donor (see Fig. 5, ●).

The specification does not enable detection methods specific for administered probes for "reactive oxygen species", or specific for administered probes which are oxidized by *in vivo* antibody-generated oxygen. Specifically:

1. The specification provides no direction for performing a method commensurate in scope to the claimed invention. None of the analytical instruments and techniques described in the specification (see *generally*, Specification, p. 24, lines 9-13) were applied to the claimed method for detecting administered probes for "reactive oxygen species", or for detecting administered probes which were oxidized by *in vivo* antibody-generated oxygen. The specification provides no working examples evidencing any of the aforementioned probes (*i.e.*, Amplex® Red, tris carboxyethyl phosphine, indigo carmine) or any of the probes listed in claims 3 or 13 (*i.e.*, vinylbenzoic acid, indigo carmine, stilbene, cholesterol) being oxidized *in vivo* by antibody-generated oxygen.
2. Prior art antibody-generated "reactive oxygen species" did not have the requisite redox potential *in vivo* to produce detectable oxidized probes. For example, Hewitt *et al.*, 46 ANN. RHEUM. DIS. 866 (1987), discovered that measurements of lipid peroxidation, diene conjugate and fluorescent IgG in exudates (see Figs. 2 and 3) fail to sensitively distinguish between control rats *versus* rats administered UV-irradiated antibodies, suggesting that these antibodies are not catalyzing formation of "reactive oxygen species" to create oxidized probes (*i.e.*, oxidized lipids, dienes and IgGs) to any significant level of detection.

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3. Prior art attempts to attribute reactive oxygen generation to antibodies are/were not successful due to background *neutrophil*-generated reactive oxygen. For example, Aaku *et al.*, 1052 BIOCHIM. BIOPHYS. ACTA 243 (1990), discovered that *neutrophils* generate reactive oxygen species, even in the absence of antibodies (see Fig. 2, ●), suggesting that antibodies merely cause degranulation of redox mediators that contribute to *neutrophil*-generated reactive oxygen redox processes (see Fig. 2, x).

Based on the foregoing, undue experimentation is necessary to re-make and practice the claimed invention.



***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 5, 7-12, 15 and 17-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Hewitt *et al.*, 46 ANN. RHEUM. DIS. 866 (1987).

Hewitt *et al.* describe methods for detecting immunological or inflammatory responses in mammals, the method comprising:

- (a) administering a probe to the mammal (see Abstract, second sentence, “A rat model of synovitis was established and challenged with both normal and free radical altered IgG”);
- (b) obtaining a sample from the mammal (see Abstract, fourth sentence, “reisolation”); and
- (c) detecting an oxidized probe in the sample (see Abstract, fourth sentence, “showed the characteristic fluorescence associated with free radical damage”);

wherein the oxidized probe indicates peroxy radicals (see Abstract, fourth sentence, “peroxidation”)

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 11 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 5, 6, 11, 15 and 16 of copending Application No. 10/534574. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The 10/534574 application also describes a method for detecting an immune response in a mammal comprising:

- (a) administering a chemical probe (see claims 1 and 11, step a) for reactive oxygen;
- (b) obtaining a sample from the mammal (see claims 11, step b); and
- (c) detecting an oxidized chemical probe thereby detecting an immune/inflammatory response (see claims 5, 6, 15 and 16).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not been patented.

***Response to Arguments***

*Claim Objections*

In prior Office Action, claims 5, 6, 15 and 16 were objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of base claims 1 and 11. This objection has been principally withdrawn.

*Claim Rejections - 35 USC § 112*

In prior Office Action, claims 1 and 11 were rejected under 35 U.S.C. 112, second paragraph, for various reasons. The rejection has been principally withdrawn.

*Claim Rejections - 35 USC § 102*

In prior Office Action, claims 1-3 and 5-10 were rejected under 35 U.S.C. 102(b) as being anticipated by Iribarren *et al.*, 17 ARTERIOSCLER. THROMB. VASC. BIOL. 1171 (1997). The rejection has been principally withdrawn.

In prior Office Action, claims 1-3, 5-13 and 15-20 were rejected under 35 U.S.C. 102(b) as being anticipated by Medford *et al.* (US 5,846,959). The rejection has been principally withdrawn.

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***Conclusion***

Claims 3, 6, 13 and 16 are free of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DAVID J. VENCI whose telephone number is (571)272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Art Unit 1641

/Long V Le/  
Supervisory Patent Examiner, Art Unit 1641